REMARKS

In response to the Final Office Action (dated July 11, 2006), Applicant filed a first Amendment and Response pursuant to 37 C.F.R. § 1.116 on September 11, 2006. As indicated in the first Advisory Action (dated October 12, 2006), the first Amendment and Response was not entered. Accordingly, Applicant filed a second Amendment and Response pursuant to 37 C.F.R. § 1.116 (dated July 11, 2006). As indicated in the second Advisory Action (dated December 11, 2006), the second Amendment and Response was entered, but fails to place the application in condition for allowance. Accordingly, Applicant is filing herewith a Request for Continued Examination, as well as the present third Amendment.

Claims 1, 6-12 were pending in the application. Claim 1 has been amended to insert the word "the" before monomeric IgA and new claim 34 has been added. Accordingly, claims 1, 6-12 and 34 are pending in the application.

New claim 34 is drawn to a portion of monomeric IgA that binds to FcαRI, linked to an agent which specifically binds the target cell or antigen, wherein the portion of monomeric IgA and the agent are linked by chemical conjugation or non-natural recombinant genetic fusion. Support for new claim 34 can be found in the present specification, at least, for example, at page at page 13, lines 1-7 of specification. Support for new claim 34 can also be found in U.S. Patent 5,922,845 at column 2, lines 26-29 and column 15, lines 8-27; and U.S. Patent 6,018,031 at column 14, lines 57-62 (both of which are explicitly incorporated by reference into the present specification at page 13, lines 4-7).

No new matter has been added. Any amendment and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was performed solely in the interest of expediting prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Acknowledgment of the Examiner's Withdrawal of Certain Rejections and Objections

Applicant gratefully acknowledges the Examiner's withdrawal of the following rejections: (a) The previous objection to the specification for various informalities; (b) The previous rejection of claims 1, 6, 8 and 11-12 under 35 U.S.C. § 102(b) as being anticipated by Mannhalter *et al.* (U.S. Patent 5,808,000, issued 9/15/1998); (c) The previous rejection of claim

1, 6, 8-11, 26-27 and 29-32 under 35 U.S.C. § 102(b) as being anticipated by van Spriel *et al.* (*Journal of Infectious Diseases*, 179(3):661-669, 3/3/1999) as evidenced by Van Egmond *et al.* (*Nature Medicine*, 6(6):68-685, June 2000); (d) The previous rejection of claims 1, 6-12 and 26-33 under 35 U.S.C. § 102(e) as being anticipated by Deo *et al.* (U.S. Patent 5,922,845, filed 7/11/1996) as evidenced by Van Egmond *et al.* (*Nature Medicine*, 6(6):68-685, June 2000); and (e) The previous rejection of claims 25-33 are rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter.

Mannhalter et al.

As indicated above, Applicant gratefully acknowledges the Examiner's withdrawal of the he previous rejection of claims 1, 6, 8 and 11-12 under 35 U.S.C. § 102(b) as being anticipated by Mannhalter *et al.* (U.S. Patent 5,808,000, issued 9/15/1998).

Further, to the extent that this rejection pertains to new claim 34, Applicant respectfully traverses. New claim 34 encompasses portions of monomeric IgA that bind to FcαRI and which are linked to an agent which specifically bind the target cell or antigen by chemical conjugation or non-natural recombinant genetic fusion. Mannhalter *et al.* neither teach nor suggest chemically linking portions of monomeric IgA to another molecule, nor fusing such molecules by *non-natural* recombinant genetic fusion, as claimed. Accordingly, new claim 34 is novel in view of Mannhalter *et al.*

Rejection of Claims 1 and 6-12 Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 6-12 are rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter. Despite the Examiner's acknowledgement that "the specification does disclose that the first portion of the complex comprises monomeric IgA," the Examiner states that the present specification "criticizes and discourages the use of monomeric IgA or portions thereof that binds FcαRI." Specifically, the Examiner relies on portions of Applicant's specification which describe the use of binding molecules which do not interfere with the binding of the natural ligand, IgA.

Applicant respectfully traverses this rejection. As set forth in Applicant's previous response, it clear from the specification, that the invention is based on the discovery that monomeric (serum) IgA binds to FcαR-expressing cells and causes elimination (*e.g.*,

phagocytosis) of antigens bound to monomeric IgA (see, for example, the first paragraph of the Summary of the Invention at page 2, lines 20-26). Accordingly, the very focus of the present application is to harness this feature of monomeric IgA to eliminate a target cell or antigen from the circulatory system of a subject, as currently claimed. Indeed, the use of monomeric IgA within the claimed complexes is not only clearly and explicitly contemplated within the four corners of the present specification, but also is the central aspect of the invention.

In particular, the specification explicitly teaches methods for eliminating a target cell or antigen using a complex which has a first portion that binds FcαRI expressed on Kupffer cells. As further taught in the specification, the first portion can include various molecules, such as monomeric IgA itself or molecules which bind to monomeric IgA; see, for example, page 3, lines 1-6, which state that "[i]n a particular embodiment of the invention, the first portion of the complex comprises serum (monomeric) IgA . . . In another embodiment, the first portion of the complex comprises an antibody, or fragment thereof, which specifically binds FcαRI or which specifically binds monomeric IgA . . ." (emphasis added).

Further evidence that monomeric IgA itself, as claimed, is supported by the present specification is provided, for example, at the following locations where Applicant refers to monomeric IgA as the first portion of the complex that "binds FcαRI"

- page 3, lines 28-32;
- page 3, line 37 through page 4, line 2;
- page 14, lines 22-25; and page 14, lines 30-33.

Moreover, original claim 3 explicitly recites that "the first portion of the complex comprises monomeric IgA."

With respect to the Examiner's statement that "the specification also makes clear that the first portion of the complex binds a site on the FcαR that is distinct from the natural binding site for IgA...and it is likely that serum IgA (up to 4.0 mg/ml may interfere with the activity of IgA mAbs under physiological conditions" (citing Applicant's specification at page 9, lines 7-9), Applicant respectfully notes that binding at a site distinct from the natural ligand is an alternative embodiment of the present invention, which in no way diminishes support for the claimed invention which encompasses monomeric IgA.

While it is true that certain embodiments taught in the specification comprise a first portion that binds a site on the FcαR that is distinct from the binding site for IgA, the

specification does not require that all embodiments possess this limitation. In fact, Applicant teaches alternate embodiments in which the first portion is not required to bind at a site on the FcαR that is distinct from the natural binding site for IgA (see, *e.g.*, page 3, lines 1-11; page 3, line 37 through page 4, line 2; page 8, lines 24-26; page 8, lines 14-24; and page 14, lines 30-32).

Moreover, Applicant respectfully submits that the mere fact that alternative embodiments are taught within the specification does not nullify actual support for the claimed invention. As indicated above, Applicant acknowledges that the specification does teach certain embodiments wherein the antibody "bind[s] outside the natural ligand binding domain of the trigger receptor" (see, *e.g.*, page 2, line 33-36). However, the Examiner misconstrues the statement in Applicant's specification "that serum IgA (up to 4.0mg/ml) ***may*** interfere with the activity of IgA mAbs under physiological conditions" as criticizing, discrediting or otherwise discouraging the presently claimed methods" (emphasis added). To the contrary, this statement simply reinforces the fact that the present specification teaches alternate embodiments, *i.e.*, embodiments which require that the first portion bind at a site on the FcαR that is distinct from the natural binding site for IgA and embodiments which do not require this limitation.

Further, while the specification acknowledges at page 9, lines 7-10 that serum IgA (*i.e.*, monomeric IgA) "***may*** interfere" with IgA mAbs by competing for binding to FcαRI, the specification does not state or even suggest that serum IgA is unable to or altogether prevented from binding to FcαRI. In fact, Applicant reiterates several times throughout the specification that monomeric IgA does indeed bind FcαRI (see *e.g.*, page 3, lines 28-32; page 3, line 27 through page 4, line 2; page 14, lines 22-25; page 14, lines 30-33). Accordingly, the mere fact that Applicant recognizes that monomeric IgA ***may*** compete with IgA mAbs in no way criticizes, discredits, or otherwise discourages the presently claimed methods.

The Examiner further asserts that

> [t]he specification as filed appears to disclose (a) the administration of serum IgA (monomeric) complexed with antigen as causing the elimination of antigens bound to monomeric IgA and (b) bispecific molecules that bind 'outside the natural ligand binding domain of the trigger receptor'...Further, applicant's reference to a complex that comprises monomeric IgA linked to a chemotherapeutic agent (specification at page 14, lines 22-25) and applicant's reference to the specification (page 6) and the working examples (pages 15-21) which disclose the use of monomeric IgA complexed with a bacteria does not

> provide adequate written support for monomeric IgA linked to an antibody (i.e., agent) that binds the target cell or antigen because a chemotherapeutic agent would not be considered an agent that binds a target cell or antigen and the claims are not limited to monomeric IgA complexed with an antigen (i.e., bacteria).

Contrary to the Examiner's assertion, the disclosure of monomeric IgA complexed with a bacteria does indeed provide adequate written description for a complex comprising monomeric IgA that binds to FcαRI, linked to an agent which specifically binds the target cell or antigen. As was well known in the art at the time the present application was filed, antigens (*i.e.*, bacteria) are recognized and bound by immune cells and, therefore, are capable of serving as the second binding specificity. That is, the claimed complex (which comprises monomeric IgA and an agent (*i.e.*, bacteria) which specifically binds the target cell or antigen) has affinity for and is capable of binding at least two different entities. Moreover, as discussed above, the specification explicitly teaches that the second binding portion of the complex, *i.e.*, agent which specifically binds the target cell or antigen, can be an antibody, or fragment thereof (see e.g., page 3, lines 7-9 and page 12, lines 33-35 of the specification). As such, there is clear written support for monomeric IgA linked to an agent that binds the target cell or antigen.

The Examiner further relies on M.P.E.P. § 2163(I)(A) and asserts that the there is insufficient written description for the present invention because "Federal Circuit has pointed out that under United States law, a description that does not render a claimed invention obvious cannot sufficiently describe the invention for purposes of the written description requirement of 35 U.S.C. § 112", *Eli Lilly*, 119 F.3d at 1567 (Fed. Cir. 1997).

Contrary to the Examiner's assertion, Applicant respectfully submits that the specification, as originally filed, fully describes the claimed invention and satisfies the foregoing proposition of law. In *Eli Lilly* (cited above by the Examiner), the court found that there was insufficient written description for a claimed nucleotide sequence because the specification did not teach the cDNA sequence and instead only taught "a general method of producing human insulin cDNA and a description of the human insulin A and B chain amino sequences that cDNA encodes." The court emphasized that the disclosure of an amino acid sequence of a protein does not render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein. In contrast, the presently claimed invention in not drawn to an undefined nucleotide

sequence, but is instead drawn to methods which encompass a complex that is clearly described and exemplified in the specification, as discussed in detail above. In accordance with the proposition set forth in *Eli Lilly*, Applicant's possession of the claimed invention would be readily apparent and obvious to one of ordinary skill in the art based on the teachings in Applicant's specification.

Finally, Applicant respectfully disagrees with the Examiner's objection to the lack of working examples which involve administration of monomeric IgA, as claimed. As discussed in Applicant's Amendment and Response dated September 11, 2006, the substance of which is reiterated herein, working examples are not a prerequisite to satisfy the written description requirement under U.S. patent law. *Falko-Gunter Falkner et al. v. Stephen Inglis et al.*, Case Nos. 05-1324 (May 26, 2006) (Gajarsa J.) (hereinafter "Falko-Gunter Falkner *et al.*") In Falko-Gunter Falkner *et al.* the Federal Circuit held that "examples are not necessary to support the adequacy of written description" and that "the written description standard may be met...even where actual reduction to practice of an invention is absent." Accordingly, a lack of exemplification of the claimed method is an insufficient basis to conclude that the present invention does not satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Based on Applicant's teachings in the specification, one of ordinary skill in the art would recognize that Applicant was in possession of the claimed invention. Accordingly, since the subject matter of the pending claims is described in accordance with 35 U.S.C. §112, first paragraph, Applicant respectfully requests that the Examiner reconsider and withdrawn the foregoing rejection.

CONCLUSION

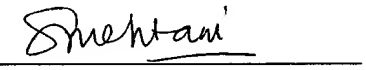
It is respectfully submitted that the entering of the Amendment would allow the Applicant to reply to the rejections raised in Advisory Action (dated December 11, 2006) and place the application in condition for allowance.

Should the Examiner feel that a telephone conference with Applicant's Attorney would expedite prosecution of the application and allowance of the claims, the Examiner is urged to contact the undersigned representative at (617) 227-7400.

Applicant submits herewith the requisite fee associated with the filing of this Amendment. However, should any additional fee be due, please charge such fee to our Deposit Account No. 12-0080, under Order No. MXI-170RCE, from which the undersigned is authorized to draw.

Dated: January 2, 2007

Respectfully submitted,

By 

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